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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,193	MIYAZAWA ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-13,71-75,92 and 93* is/are rejected.

7)☒ Claim(s) *1 and 3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,3,4,8-14,16,17,22,26,29,31,35,38-40,44,45,47,48,50-54,57-59,61-65,67,68 and 70-93.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 14,16,17,22,26,29,31,35,38-40,44,45,47,48,50-54,57-59,61-65,67,68,70 and 76-91.

DETAILED ACTION

This Office Action is in response to the amendment filed 05 April 2010.

Claims 2, 5-7, 15, 18-21, 23-25, 27, 28, 30, 32-34, 36, 37, 41-43, 46, 49, 55, 56, 60, 66 and 69 have been cancelled.

Claims 92 and 93 have been added.

Claims 1, 3, 4, 8-14, 16, 17, 22, 26, 29, 31, 35, 38-40, 44, 45, 47, 48, 50-54, 57-59, 61-65, 67, 68 and 70-93 are pending.

Claims 14, 16, 17, 22, 26, 29, 31, 35, 38-40, 44, 45, 47, 48, 50-54, 57-59, 61-65, 67, 68, 70 and 76-91 are withdrawn from further consideration pursuant to 37 CFR 1.142(b). The previous Office Action mailed on 05 October 2009 contained typographical errors in omitting withdrawn claims 76-91 and in stating that claim 4 was withdrawn, which should have been claim 14. Examiner apologizes for her oversight.

Claims 1, 3, 4, 8-13, 71-75, 92 and 93 are currently examined.

Objections

(Prior Objection – Maintained) The objection to claim 1 is maintained because of the following informalities:

(1) Applicant's amendment adds the phrase "HIV virus" in the second line. The "virus" is redundant because HIV is an acronym for human immunodeficiency virus;

(2) The acronym "HIV" is not identified by its full name at its first appearance; and

(3) The "&" between "D22S423" and "D22S418" should be replaced with a comma.

(New Objection) Claim 3 is objected to because of the following informalities:

(1) the claim is missing a space between the words "D22S1169" and "or" in the fourth line;

(2) The "&" between "D22S423" and "D22S418" should be replaced with a comma.

(New Objection) Claim 71 is objected to because of the phrase "who are indicative of a resistance to infection," which should be "who are resistant to infection."

(New Objection) The disclosure is objected to because of the following informalities: there is no brief description of Figure 8 in the drawings.

Appropriate correction is required.

Duplicate Claims

Applicant is advised that should claim 71 be found allowable, the newly added claim 92 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(Prior Rejection – Maintained) The provisional nonstatutory obviousness-type double patenting rejection of claims 1, 3, 4, 71 and new claims 92 and 93 as being

unpatentable over claims 50-54 and 61-63 of US application No. 11/793,575 is maintained until Applicants' submission of a compliant terminal disclaimer.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Indefiniteness Rejection

(Prior Rejection – Withdrawn) The rejection of claim 71 under 35 U.S.C. §112, second paragraph, as being indefinite is withdrawn upon consideration of the limitations in the base claim.

Written Description Rejection

(Prior Rejection – Maintained) Claims 1, 3, 4, 8-13, 71-75 and new claims 92 and 93 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is maintained for the following reasons:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings or structural chemical formulas, or by disclosure of relevant, identifying characteristics, *i.e.*, complete/partial structure or other physical

and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, by predictability in the art, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Claims 1, 3, 4, 8-13, 71-75, 92 and 93 are drawn to a method of determining resistance to HIV infection comprising identifying alleles present at the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169. Claim 3, 13, 71 and 75 is also drawn to identifying presence of a nucleic acid sequence, complementary nucleic acids or fragments, homologues, splice variants, polymorphisms, genotypes, or derivatives of microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169. The claims do not limit the size or the sequence structure of the allele, variant, homologue, complement, and derivative. Thus, the instant claims recite a broad genus of highly variable nucleic acid sequences.

In *Regents of the University of California v. Eli Lilly and Co.* 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the Court decided that adequate written description of genetic material "requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." *Id.* 43 USPQ2d at 1404 (quoting Fiefs, 984 F.2d at 1171, 25 USPQ2d at 1606). The cited case law is relevant to the instant invention because there is limited disclosure of the structure, formula, or physical properties of a " homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" of an allele

or genotype at the recited microsatellite loci and there is only a disclosure of the functional characteristic of the "allele, homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" as a genetic marker for infection resistance, rather than of what it is.

In the instant case, the claims are drawn to a genus of highly variable nucleic acids that is defined only by the function as a genetic marker for resistance to infection. The specification only provides description for homology between mouse chromosome 15 containing Rfv3 and human chromosome 22. There is reduction to practice of four alleles: (1) an allele with the size of 134 base pairs (bp) at D22S272 and (2) allele 221bp at D22S423, which frequencies are significantly different in the HIV-exposed but un-infected group when compared to the healthy control group and the HIV-infected group (see Table 4 on page 38), and (3) allele size 156bp and (4) allele 158bp at the D22S277 locus, which frequency showed significant difference in the HIV-exposed but un-infected group when compared to the combined healthy control and HIV-infected group (spec. p. 31, lines 13-21). These alleles or genotypes, however, do not share any common partial structure that can be correlated with the function of HIV infection resistance. Therefore, the specification does not identify any partial structural features or motifs that correspond to the functional limitation of resistance to HIV infection.

Importantly, the specification does not disclose the structural patterns with allele size constraints correlated to functional significance at these microsatellite loci. The specification does not disclose a representative number of species of the "homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" of the

alleles at microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169, either. There is a high level of unpredictability in the function of the alleles and its homologues, splice variants, polymorphisms, derivatives, complementary nucleic acids or fragments at the recited microsatellite markers since the rates of microsatellite mutation are much higher than those of point mutation at coding genes (Li *et al.*, 2002). The mutation rates at microsatellites vary among loci and mutation patterns of the allele sequences are so complex (Jin *et al.*, 1996) that the functions of these genetic markers cannot be tightly and predictably linked to their homologues, splice variants, derivatives, complementary nucleic acids and fragments.

As a result, one of skill in the art could not conclude that Applicant was in possession of the claimed genus of alleles, genotypes, homologues, splice variants, polymorphisms, derivatives, complementary nucleic acids or fragments in the claimed method at the time of the invention without any description of the structural patterns with allele size constraints correlated to functional significance at these microsatellite loci. Therefore, claims 1, 3, 4, 8-13, 71-75, 92 and 93 do not meet the written description provision of 35 U.S.C. §112, first paragraph.

Response to Arguments

As set forth above, the rationale of the instant rejection and factor analysis have been modified accordingly to address the amended claims. Applicant's arguments filed 05 April 2010 have been fully considered but they are not persuasive. Applicants argue that Applicants' specification clearly describes methods of determining a predisposition

or resistance to infection by obtaining a DNA bearing sample from a subject, and assaying the sample to identify the alleles present at microsatellite loci. Applicants further argue that the finding of allele 221 at the D22S423 loci, alleles 156 and 158 at D22S277 loci provide strong evidence that genotypes at this segment of chromosome 22 are associated with enhanced immune responses to HIV-1 in uninfected individuals.

Although the specification describes the method of assay a DNA sample to identify the alleles present at microsatellite loci, the specification does not clearly disclose the structural patterns with size constraints of all the alleles present at all the recited microsatellite loci that are correlated with the functional significance to resistance to HIV infection. As set forth in the Office Action mailed 05 October 2009 and reiterated above, an adequate written description of genetic material "requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention. *Regents of the University of California v. Eli Lilly and Co.* 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The instant rejection is not based on whether one skilled in the art would know how to sequence or assay a DNA sample to identify alleles present at these microsatellite loci, but rather, the non-existent correlation of the structures of the claimed vast genus with the function of HIV resistance.

The disclose of allele 221 at D22S423 and alleles 156 and 158 at D22S277 is not sufficient to represent all the other allele species present at the recited microsatellite loci at this segment of chromosome 22 because of the lack of description of any genotype structure or formula that is correlated with the function of HIV resistance. For the same

reason, when viewed together with the state of art pertaining to the high level of unpredictability in microsatellites and their functional significance, the lack of description of any homologues, splice variants, polymorphisms, derivatives, complementary nucleic acids or fragments of the alleles at the recited microsatellite markers does not place the applicants in possession of the genus.

Scope of Enablement Rejection

(Prior Rejection – Maintained) Claims 1, 3, 4, 8-13, 71-75 and new claims 92 and 93 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not enabled by the specification commensurate in scope is maintained for the following reasons:

Claims 1, 3, 4, 8-13, 71-75, 92 and 93 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for determining resistance to HIV infection comprising assaying or sequencing a DNA sample to identify the presence of allele 134 at D22S272, allele 221 at D22S423 and alleles 156 and 158 at D22S277, does not reasonably provide enablement for determining resistance to HIV infection using any other allele or using any homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112, first paragraph, the courts have put forth a series

of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

Nature of the invention. The claims are drawn to a method of determining a resistance to HIV infection comprising assay a DNA bearing sample from a subject to detect allele presence of at least one of the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169.

Breadth of the claims. The instant claims encompass determining resistance to HIV infection with any allele at the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. Claim 3 further encompasses homologues, splice variants, complementary nucleic acids, or derivatives of the microsatellite loci at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. The claimed microsatellite allele/nucleic acid sequence/homologues, splice variants or derivatives are not limited to a single nucleic acid sequence, encompassing use of a wide variety of sequences encoding uncharacterized proteins.

Working examples. The disclosure fails to provide any working embodiments that meet the claimed limitations. There is an example showing linkage between Friend

leukemia virus-neutralizing antibody titer in mice and single-stranded length polymorphism (SSLP) analysis of genotypes at the mouse chromosome 15 locus of the *Rfv*-3 gene, the mouse gene that confers resistance to Friend's virus infection (see page 19-21 and 23-25, paragraph [0072]-[0074], [0076], and [0078]-[0082]). There is another example showing SSLP genotype analysis of HIV-exposed but serum-negative/un-infected human subjects with human microsatellite markers that are syntenic with the mouse microsatellite markers (see page 20-22 and 25-27, paragraph [0075], [0077], [0083]-[0085]), which identified four alleles: (1) an allele with the size of 134 base pairs (bp) at loci D22S272 and (2) allele 221bp at D22S423, which frequencies are significantly different in the HIV-exposed but un-infected group when compared to the healthy control group or the HIV-infected group (see Table 4 on page 38), and (3) allele size 156bp and (4) allele 158bp at the D22S277 locus, which frequency showed significant difference in the HIV-exposed but un-infected group when compared to the combined healthy control and HIV-infected group (spec. p. 31, lines 13-21). However, no other working examples are present to show a correlation between the presence of alleles at the microsatellite marker, D22S929, D22S264, D22S418 or D22S1169, and the resistance to HIV infection. Neither is there any working example of identifying any homologue, derivative, splice variant, complementary nucleic acid or fragment of any alleles.

Guidance in the specification. The disclosure fails to provide sufficient guidance pertaining to the correlation between the genotypic presence of alleles at all of the claimed microsatellite loci and the phenotype of resistance to HIV infection. Even

though the working example teaches the DNA sequence homology between mouse chromosome 15, which contains the Friend's virus-resistance gene *Rfv3*, and the human chromosome 22 (see Figures 2, 4 and 5), the specification is limited to the association of HIV-exposed un-infected phenotype with the genotype of allele frequency at only four alleles present at three microsatellite loci, D22S277, D22S423 and D22S272 within the chromosome 22 locus (see page 31, Figure 6 or Table 4 on page 38). Actually, the specification does not even show that every claimed microsatellite loci has an allele frequency correlated with the resistance to HIV infection. As set forth by the data in Table 4 on page 38, only the D22S272 and D22S423 microsatellite markers show significant differences between the HIV-exposed un-infected (EUI) group and the infected or the healthy control (HC) group. The specification only states that when allele frequencies were compared between the three phenotypic groups, their distribution at the D22S277 locus differed between the EUI and HC groups at P= 0.039. No significant difference was observed at the other loci (page 37, lines 15-19).

The specification only discloses Applicant's hypotheses that the IgA antibodies in HIV- exposed un-infected people provide the immune response against all strains of HIV infection and that the IgA antibody-producing individuals can be determined by genotyping with the chromosome 22 microsatellite markers, which is based on the observation that exposed sero-negative individuals possess distinct rare alleles at microsatellite loci within a region of chromosome 22 that is syntenic to the area of mouse chromosome 15 containing a retrovirus resistance gene, *Rfv*-3 (page 3, lines 5-8). However, without sufficient guidance pertaining to the structural patterns with size

constraints of alleles at each microsatellite that is tightly linked to resistance to HIV infection, the skilled artisan has only been extended an undue invitation to further experimentation to ascertain which allele, homologue, splice variant, derivative, complementary nucleic acid or fragment present at which of the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 is associated with HIV resistance.

State of the prior art and Predictability. At the time the invention was made, a method of determining resistance to HIV infection by genotyping the microsatellite loci in DNA sample is not considered routine in the art. The prior art only shows that genotype analysis of an identified gene that is associated with a resistance to HIV infection, such as the APOBEC3 gene (see Sheehy *et al.*), identified by Jarmuz *et al.* to be on human chromosome 22, which is shown by Super *et al.* to share sequence homology with mouse chromosome 15 containing the Friend's virus resistance gene, Rfv3. The prior art fails to provide sufficient illumination pertaining to the correlation between a resistance to HIV infection and the presence of any allele and any homologue, derivative, splice variant, derivative, complementary nucleic acid or fragment at all of the instantly claimed microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. However, the prior art discloses an association of cancer or tumor genes with chromosome 22 microsatellite markers D22S423, D22S272, and D22S277 (see Ingvarsson *et al.*), a linkage of the manifestation of schizophrenic symptoms to polymorphism near the microsatellite marker D22S264 (see Takase *et al.*), and a correspondence of Der(22) syndrome and Velo-Cardio-Facial

Syndrome/DiGeorge Syndrome with the presence of alleles at marker D22S264 (see Funke *et al.*). In conclusion, the phenotypic or clinical manifestation of the mere presence of alleles at microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 is rather unpredictable. The genotypic result of these alleles, complementary nucleic acid, variant, homologue, or derivative alone is uninformative without detecting a specific gene that is correlated with HIV resistance and without any confirming phenotypic assays. In other words, the prior art only teaches that the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 is effective for genotype analysis of an identified gene that is associated with a specific disease condition.

Furthermore, it is known for proteins that even a single amino acid mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the recitation of "homologues, splice variants, or derivatives of the microsatellite loci" results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated function of resistance to HIV infection and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit certain specific sequences may be conserved over biomolecules of related function upon a significant amount of further research. See Pakula *et al.* (1989) and Oestreicher *et al.* (1995) for example.

Amount of experimentation necessary. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). It is not obvious from the disclosure how one can determine resistance to HIV infection with any of the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 by detecting the presence of any allele or its homologue, derivative, splice variant, complementary nucleic acid or fragment. Just as there is uncertainty in which alleles, other than those specifically identified in the specification, would be indicative of resistance to HIV infection, there would similarly be uncertainty as to which alleles would be indicative of a predisposition to HIV infection.

M.P.E.P. §2164.03 [R-2] states: [I]n applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soil*, 97 F.2d 623,624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488,496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicants argued that the claim amendment obviates the enablement rejection. Examiner however respectfully disagrees for the following reasons:

Applicant's amendment narrowing the scope of resistance to infection to resistance to HIV infection does not address all of the issues raised in the instant rejection as set forth above. The rationale of the instant rejection and Wands factor analysis has been modified according to the amendment to the rejected claims.

Examiner's analysis of the Wands factors and the articulation of reasoning provide the basis for Examiner's conclusion that the instant specification does not enable the full scope of the claimed invention. Specifically, the disclosure does not enable determining resistance to HIV infection by: (1) using microsatellite loci D22S929, D22S264, D22S418 and D22S1169; (2) identifying the presence of any allele at the recited microsatellite loci; (3) identifying the presence of homologues, splice variants, derivatives, complementary nucleic acids or fragments thereof. The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). See M.P.E.P. §2164.03 [R-2]. Relationship of Predictability of the Art and the Enablement Requirement. Applicants have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue

experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Response to Arguments

Applicant's arguments, see page 23, lines 8-11, filed 05 April 2010, with respect to claims 1, 3-13 and 71-75 have been fully considered and are persuasive. The rejections of claims 1, 3-13 and 71-75 have been withdrawn.

(Prior Rejection – Withdrawn) The rejection of claims 1, 3-12, and 71-74 under 35 U.S.C. §103(a) as being obvious over Stephens *et al.* (1998) in view of Super *et al.* (1999), Jarmuz *et al.* (14 July 2002) and Sheehy *et al.* (8 August 2002) is withdrawn in light of Applicant's argument that none of the prior references suggests the specifically recited microsatellite loci as associated with resistance to HIV infection.

(Prior Rejection – Withdrawn) The rejection of claims 13 and 75 under 35 U.S.C. §103(a) as being obvious over Stephens *et al.* (1998) in view of Super *et al.* (1999), Jarmuz *et al.* (14 July 2002), Sheehy *et al.* (8 August 2002) and Ingvarsson *et al.* (20 March 2002) is withdrawn in light of Applicant's argument that none of the prior

references suggests the specifically recited microsatellite loci as associated with resistance to HIV infection.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Primary Examiner, Art Unit 1648